

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
LAWRENCE P. CASSON
KENYON & KENYON
ONE BROADWAY
NEW YORK, NY 10004

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing
(day/month/year)

07 APR 2006

Applicant's or agent's file reference
12958/461761

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/US04/34966

International filing date
(day/month/year) 22 October 2004 (22.10.2004)

Applicant
UNIVERSITY OF PITTSBURGH

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70.

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the PCT Applicant's Guide, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/ US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (571) 273-3201

Authorized officer

Quang Nguyen, Ph.D.

Telephone No. (571) 272-1600

Form PCT/ISA/220 (January 2004)

(See notes on accompanying sheet)

EV 322 948 863 US

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 12958/461761	FOR FURTHER ACTION <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/US04/34966	International filing date (day/month/year) 22 October 2004 (22.10.2004)	(Earliest) Priority Date (day/month/year) 22 October 2003 (22.10.2003)
Applicant UNIVERSITY OF PITTSBURGH		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the language, the international search was carried out on the basis of



the international application in the language in which it was filed.

a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐

With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I

2. ☐

Certain claims were found unsearchable (See Box No. II)

3. ☒

Unity of invention is lacking (See Box No. III)

4. ☒

With regard to the title,



the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,



the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. _____



as suggested by the applicant.

as selected by this Authority, because the applicant failed to suggest a figure.

as selected by this Authority, because this figure better characterizes the invention.

b. ☒

none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

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Box No. II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-8 and 10-40

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/34966

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 5/00, 5/02, 5/08
US CL : 435/325, 371, 377

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/325, 371, 377

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	WO 00/73421 A2 (LIFEBANK SERVICES, L.L.C.) 07 December 2000, see the entire document, especially the abstract, pages 3-4; page 6, line 16 continues to line 7 of page 7; page 8, lines 10-23.	1-8, 10-24, 27-29 and 33 — 30 and 36-39
X — Y	WO 03/042405 A2 (CHILDREN'S MEDICAL CENTER CORPORATION) 22 May 2003, see the entire document, especially the abstract, pages 2-5; page 21, paragraphs 80-81; page 22, paragraph 83.	1-8, 10-23, 26-29 and 33 — 30 and 36-39
X — Y	US 2003/0180269 A1 (HARIRI, R.J.) 25 September 2003, see the entire document, especially the following paragraphs 057-077, 082-085, 114-123.	1-8, 10-29, 31-33 and 35 — 30 and 36-39
Y	US 2002/0151053 A1 (GERON CORPORATION) 17 October 2002, see the entire document, especially paragraph 109-117 and 178.	30
Y	WO 99/20741 (GERON CORPORATION) 29 April 1999, see the entire document, especially the abstract and page 3, lines 1-8.	36-39

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"B" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"Z" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

23 January 2006 (23.01.2006)

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Date of mailing of the international search report

07 APR 2006

Authorized officer

Quang Nguyen, Ph.D.

Telephone No. (571) 272-1600

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/34966

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-8 and 10-40, drawn to a composition comprising a placental stem cell isolated from the amnion or from the amniotic epithelium, a method of making and a first method of using the same for making a cardiomyocyte.

Group II, claims 41 and 43-44, drawn to a cardiomyocyte and methods of using the same for determining whether a test agent is toxic to a cardiomyocyte or for determining a metabolic product of a test agent.

Group III, claims 45-52 and 54-55, drawn to a method of making a hepatocyte, a hepatocyte and methods of using the same for determining whether a test agent is toxic to a hepatocyte or for determining a metabolic product of a test agent.

Group IV, claims 56-58 and 60-61, drawn to a method of making a pancreatic cell, a pancreatic cell and methods of using the same for determining whether a test agent is toxic to a pancreatic cell or for determining a metabolic product of a test agent.

Group V, claims 62-63 and 65-66, drawn to a method of making a neural cell, a neural cell and methods of using the same for determining whether a test agent is toxic to a neural cell or for determining a metabolic product of a test agent.

Group VI, claims 67-69 and 71-72, drawn to a method of making a vascular endothelial cell, a vascular endothelial cell and methods of using the same for determining whether a test agent is toxic to a vascular endothelial cell or for determining a metabolic product of a test agent.

Group VII, claims 9, 73 and 83-86, drawn to a pharmaceutical composition comprising a placental stem cell of the invention and a method of regenerating or restoring a metabolic function to a patient in need thereof using the same.

Group VIII, claims 42 and 74, drawn to a pharmaceutical composition comprising a cardiomyocyte of the invention and a method of regenerating or restoring a metabolic function to a patient in need thereof using the same.

Group IX, claims 53 and 75, drawn to a pharmaceutical composition comprising a hepatocyte of the invention and a method of regenerating or restoring a metabolic function to a patient in need thereof using the same.

Group X, claims 59 and 76, drawn to a pharmaceutical composition comprising a pancreatic cell of the invention and a method of regenerating or restoring a metabolic function to a patient in need thereof using the same.

Group XI, claims 64 and 77, drawn to a pharmaceutical composition comprising a neural cell of the invention and a method of regenerating or restoring a metabolic function to a patient in need thereof using the same.

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Group XII, claims 70 and 78, drawn to a pharmaceutical composition comprising a vascular endothelial cell of the invention and a method of regenerating or restoring a metabolic function to a patient in need thereof using the same.

The inventions listed as Groups I-XII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The placental stem cell composition of Group I, the cardiomyocyte composition of Group II, the hepatocyte composition of Group III, the pancreatic cell composition of Group IV, the neural cell composition of Group V, the vascular endothelial cell composition of Group VI and the pharmaceutical compositions of Groups VII-XII are different compositions that have different components that do not share the same common core structure and that they have different properties one from the others (e.g., a stem cell is different immunophenotypically and has different properties from differentiated cells such as a cardiomyocyte, a hepatocyte, a neural cell, a pancreatic cell or a vascular endothelial cell; and that a pharmaceutical composition renders therapeutic effects to a treated patient). Accordingly, these compositions lack a common utility that is based upon a common structural feature that is a basis for that common utility. Similarly, the methods of using these compositions also lack a common utility for the same reasoning.

Continuation of B. FIELDS SEARCHED Item 3:

APS, DIALOG, MEDLINE, EMBASE, BIOSIS

search terms: placental stem cell, placenta, amnion, epithelial, cardiomyocyte, Strom-Stephen.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
LAWRENCE P. CASSON
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ONE BROADWAY
NEW YORK, NY 10004

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference

12958/461761

Date of mailing
(day/month/year)

07 APR 2006

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US04/34966

International filing date (day/month/year)

22 October 2004 (22.10.2004)

Priority date (day/month/year)

22 October 2003 (22.10.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(8): C12N 5/00, 5/02, 5/08 and US Cl.: 435/325, 371, 377

Applicant

UNIVERSITY OF PITTSBURGH

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Date of completion of this opinion

05 February 2006 (05.02.2006)

Authorized officer

Quang Nguyen, Ph.D.

Telephone No. (571) 272-1600

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/34966

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing
☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper
☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.
☐ filed together with the international application in electronic form.
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/34966

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:
- ☐ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
See the lack of unity section of the International Search Report (Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-8 and 10-40

WRITTEN OPINION OF THE
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Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>30, 34 and 36-40</u>	YES
	Claims <u>1-8, 10-29, 31-33 and 35</u>	NO
Inventive step (IS)	Claims <u>34 and 40</u>	YES
	Claims <u>1-8, 10-33 and 35-39</u>	NO
Industrial applicability (IA)	Claims <u>1-8 and 1040</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Please See Continuation Sheet

Claim 30 lacks an inventive step under PCT Article 33(3) as being obvious over WO/0073421 A2 or WO03/042405 A2 or US 2003/0180269 A1 in view of US 2002/0151053 A1.

The teachings of WO/0073421 A2 or WO03/042405 A2 or US 2003/0180269 A1 were disclosed above. However, none of the references taught specifically of culturing placental stem cells with TGF-alpha.

At the effective filing date of the present disclosure, US 2002/0151053 A1 already taught culturing pluripotent stem cells in the presence of a maturation co-factor such as TGF-alpha or TGF-beta among others to obtain an enrichment of hepatocyte-like cells (paragraph 112).

It would have been obvious for an ordinary skilled artisan to use the maturation factor such as TGF-alpha taught by US 2002/0151053 A1 in the cultured multipotential stem cell populations of either WO/0073421 A2 or WO03/042405 A2 or US 2003/0180269 A1 since they all taught to differentiate the stem cells to any cell lineages using known differentiation agents.

The cultured multipotential stem cell populations under TGF-alpha would result in enriched cells in a composition as broadly claimed.

Accordingly, claim 30 lacks an inventive step for the reasons discussed above.

Claims 36-39 lack an inventive step under PCT Article 33(3) as being obvious over WO/0073421 A2 or WO03/042405 A2 or US 2003/0180269 A1 in view of WO 99/20741.

The teachings of WO/0073421 A2 or WO03/042405 A2 or US 2003/0180269 A1 were disclosed above. However, none of the references taught specifically of culturing placental stem cells under subatmospheric ambient oxygen conditions.

At the effective filing date of the present disclosure, WO 99/20741 already taught culturing primate-derived primordial stem cells in a substantially undifferentiated state in a cell culture medium that has an osmotic pressure of less than about 300 mOsm/kg, preferably about 280 mOsm/kg.

It would have been obvious for an ordinary skilled artisan to use the low osmotic culture condition taught by WO 99/20741 to grow and expand the multipotential stem cells of WO/0073421 A2 or WO03/042405 A2 or US 2003/0180269 A1 in a substantially undifferentiated state as needed by the artisan.

The multipotential stem cell populations cultured under the low osmotic culture condition would result in enriched cells in a composition as broadly claimed.

Accordingly, claims 36-39 lack an inventive step for the reasons discussed above.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:

Claims 1-8, 10-24, 27-29 and 33 lack novelty under PCT Article 33(2) as being anticipated by WO 00/73421 A2.

WO 00/73421 A2 disclosed a method for isolating, culturing human amniotic epithelial cells derived from placenta at delivery as well as methods for inducing differentiation of these multipotential cells and manipulating the cells by gene transfection (see abstract, pages 3-4 and 9). Selective adhesion techniques are taught to be used to eliminate mesenchymal fibroblasts in the isolation of human amniotic epithelial cells (page 6, lines 9-10). The human amniotic epithelial cells are characterized by round, cobblestone morphology, large nuclei, epithelial membrane antigen and cytokeratin staining, and gap junctional communication (page 6, lines 13-15). The isolated amniotic epithelial cells are cultured in various media such as DMEM, F-12, M199, supplemented with fetal bone serum, whole human serum or human umbilical cord serum or supplemented with growth factors, cytokines, hormones, vitamins or any combination thereof. Additionally, the amniotic epithelial cells are cultured on feeder cells, such as irradiated fibroblasts (page 6, lines 16-26). Agents such as EGF, aFGF, bFGF, PDGF, KGF, TGF-beta, retinoic acid, insulin, prolactin, TPA, DMSO, androgen, estrogen, cytokines and others can be used to induce differentiation of the amniotic epithelial cells (page 7, first paragraph; page 8, lines 15-23).

Since the multipotential human amniotic epithelial cells disclosed in WO 00/73421 A2 are derived from the same tissue source, isolated and cultured by a similar method, and in light of their disclosed characteristics, it is inherent that the multipotential amniotic epithelial cells also possess the same characteristics as the cell compositions of the present invention.

Accordingly, the instant claims are anticipated by WO 00/73421 A2.

Claims 1-8, 10-23, 26-29 and 33 lack novelty under PCT Article 33(2) as being anticipated by WO 03/042405 A2.

WO 03/042405 A2 disclosed methods of isolation, expansion and differentiation of pluripotent fetal stem cells from chorionic villus, amniotic fluid and placenta (see abstract). The fetal stem cells are also manipulated by gene transfection for therapeutic applications (page 3, paragraph 9). The isolated pluripotent human fetal stem cells are used to differentiate to cells of different lineages, including but not limited to osteogenic, adipogenic, myogenic, neurogenic, hematopoietic and endothelial lineages by exposing the stem cells to one or more differentiation-inducing agents such as BGF, aFGF, bFGF, PDGF, KGF, TGF-P, retinoic acid, insulin, prolactin, DMF, androgen, estrogen, cytokines and others (paragraphs 81 and 83). Antibodies reactive to c-kit are used to isolate the human fetal stem cells (paragraph 42). Fetal stem cells are cultured in various media such as DMEM, F-12, MI 99 supplemented with fetal bovine serum, whole human serum or supplemented with growth factors, cytokines, hormones, vitamins, antibiotics or any combination thereof (paragraph 80). WO 03/042405 A2 further disclosed that most of the isolated cells from chorionic villi and amniotic fluid were of epithelial origin and stained positively for cytokeratins (paragraph 98).

Since the pluripotent fetal stem cells disclosed in WO 03/042405 A2 are derived from the same tissue source, isolated and cultured by a similar method, and in light of their disclosed characteristics, it is inherent that the pluripotent fetal stem cells also possess

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INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/34966

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

the same characteristics as the cell compositions of the present invention.
Accordingly, the instant claims are anticipated by WO 03/042405 A2.

Claims 1-8, 10-29, 31-33 and 35 lack novelty under PCT Article 33(2) as being anticipated by Hariri (US 2003/0180269 A1).

Hariri provides compositions comprising embryonic-like stem cells that originate from an extract or perfusate of a exanguinated post-partum placenta, the cells are characterized by the presence of surface markers OCT-4, ABC-p, SH2, SH3, SH4, CD90 and the absence of CD34, CD38, CD45, SSEA3 and SSEA4 (see abstract, paragraph 17). Hariri also teaches that the embryonic-like stem cells are treated with a growth factor, a cytokine or an interleukin to induce cell differentiation (paragraph 47). The embryonic-like stem cells are isolated from the effluent perfusate from a cultured placenta using techniques known by those skilled in the art, such as, density gradient centrifugation, magnet cell separation, flow cytometry or other cell separation or sorting methods well known in the art (paragraphs 65-69 and 77). The isolated embryonic-like stem cells can be cultured on feeder cells such as irradiated fibroblasts, expanded and cultured and induced differentiation in the presence of agents such as EGF, KGF, retinoic acid, hormones, and others (paragraphs 79, 82). The embryonic-like stem cells can also be genetically modified using a recombinant viral and non-viral vector containing a transgene (paragraphs 114-116).

Since the embryonic-like stem cells derived from the same tissue source, isolated and cultured by a similar method, and in light of their disclosed characteristics, it is inherent that the embryonic-like stem cells of Hariri also possess the same characteristics as the cell compositions of the present invention.

Accordingly, the instant claims are anticipated by Hariri (US 2003/0180269 A1).